



AMENDMENT TO THE CLAIMS

Please add new claims 20 and 21, and amend claims 14 and 17 as shown in the following list of claims:

1.-13. (Canceled).

14. (Currently Amended) A method of inhibiting TfR binding to transferrin, comprising administering to a subject a therapeutically effective amount of a compound comprising the formula:

(I) $Z_1-X_1-X_2-X_3-X_4-X_5-X_6-X_7-X_8-X_9-X_{10}-X_{11}-X_{12}-X_{13}-X_{14}-X_{15}-X_{16}-X_{17}-Z_2$

wherein:

X_1 is an apolar residue;

X_2 is a hydrophobic residue;

X_3 is an acidic or an aliphatic residue;

X_4 is a basic residue;

X_5 is an apolar residue;

X_6 is an aromatic residue;

X_7 is a polar residue;

X_8 is an aliphatic residue;

X_9 is an acidic or an aliphatic residue;

X_{10} is an aromatic residue;

X_{11} is an aromatic residue;

X_{12} is a polar residue;

X_{13} is Ile;

X_{14} is an apolar residue;

X_{15} is an acidic residue;

X_{16} is a polar residue;

X_{17} is a basic or an aliphatic residue;

Z_1 is H_2N^- , RHN^- or, RRN^- ;

Z_2 is $-C(O)R$, $-C(O)OR$, $-C(O)NHR$, or $-C(O)NRR$;

each R is independently (C_1-C_6) alkyl, (C_1-C_6) alkenyl, (C_1-C_6) alkynyl, substituted (C_1-C_6) alkyl, substituted (C_1-C_6) alkenyl or substituted (C_1-C_6) alkynyl;

each " " between residues Z_1 and X_1 and residues Z_2 and X_{17} represents a covalent linkage; and

each "—" between residues X₁ through X₁₇ represents a covalent linkage,
wherein the compound reduces cell-associated binding of transferrin as measured in
an *in vitro* cellular binding assay and produces at least an additive effect with soluble
HFE/ β_2 m heterodimers in reducing cell-associated binding of transferrin as measured in the
assay.

15. (Previously Added) The method of Claim 14, wherein:

- X₁ is an apolar amino acid;
- X₂ is an aromatic amino acid;
- X₃ is an acidic amino acid;
- X₄ is a basic amino acid;
- X₅ is an apolar amino acid;
- X₆ is an aromatic amino acid;
- X₇ is a polar amino acid;
- X₈ is a aliphatic amino acid;
- X₉ is a an acidic amino acid;
- X₁₀ is an aromatic amino acid;
- X₁₁ is an aromatic amino acid;
- X₁₂ is a polar amino acid;
- X₁₃ is Ile;
- X₁₄ is an apolar amino acid;
- X₁₅ is an acidic amino acid;
- X₁₆ is a polar amino acid;
- X₁₇ is a basic amino acid; and

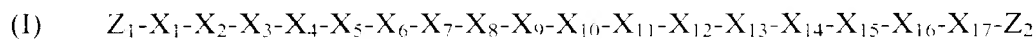
each "—" between residues X₁ through X₁₇ is independently an amide, a
substituted amide or an isostere of amide.

16. (Previously Added) The method of Claim 14, wherein:

- X₁ is Gly;
- X₂ is Trp or Ala;
- X₃ is Asp or Ala;
- X₄ is His;
- X₅ is Met;
- X₆ is Phe;

X_7 is Thr;
 X_8 is Val;
 X_9 is Asp or Ala;
 X_{10} is Phe;
 X_{11} is Trp;
 X_{12} is Thr;
 X_{13} is Ile;
 X_{14} is Met;
 X_{15} is Glu;
 X_{16} is Asn;
 X_{17} is His or Ala;
 Z_1 is H_2N- ;
 Z_2 is $-C(O)OH$; and
 each "—" between residues X_1 through X_{17} is an amide linkage.

17. (Currently Amended) A method of treating an iron overload disease, comprising administering to a subject a therapeutically effective amount of a compound comprising the formula:



wherein:

X_1 is an apolar residue;
 X_2 is a hydrophobic residue;
 X_3 is an acidic or an aliphatic residue;
 X_4 is a basic residue;
 X_5 is an apolar residue;
 X_6 is an aromatic residue;
 X_7 is a polar residue;
 X_8 is an aliphatic residue;
 X_9 is an acidic or an aliphatic residue;
 X_{10} is an aromatic residue;
 X_{11} is an aromatic residue;
 X_{12} is a polar residue;
 X_{13} is Ile;
 X_{14} is an apolar residue;

X_{15} is an acidic residue;
 X_{16} is a polar residue;
 X_{17} is a basic or an aliphatic residue;
 Z_1 is H_2N- , $RHN-$ or, $RRN-$;
 Z_2 is $-C(O)R$, $-C(O)OR$, $-C(O)NHR$, or $-C(O)NRR$;
each R is independently (C_1-C_6) alkyl, (C_1-C_6) alkenyl, (C_1-C_6) alkynyl, substituted (C_1-C_6) alkyl, substituted (C_1-C_6) alkenyl or substituted (C_1-C_6) alkynyl;
each "—" between residues Z_1 and X_1 and residues Z_2 and X_{17} represents a covalent linkage; and
each "—" between residues X_1 through X_{17} represents a covalent linkage,
wherein the compound reduces cell-associated binding of transferrin as measured in an in vitro cellular binding assay and produces at least an additive effect with soluble HFE/ β_2m heterodimers in reducing cell-associated binding of transferrin as measured in the assay.

18. (Previously Added) The method of Claim 17, wherein:

X_1 is an apolar amino acid;
 X_2 is an aromatic amino acid;
 X_3 is an acidic amino acid;
 X_4 is a basic amino acid;
 X_5 is an apolar amino acid;
 X_6 is an aromatic amino acid;
 X_7 is a polar amino acid;
 X_8 is a aliphatic amino acid;
 X_9 is a an acidic amino acid;
 X_{10} is an aromatic amino acid;
 X_{11} is an aromatic amino acid;
 X_{12} is a polar amino acid;
 X_{13} is Ile;
 X_{14} is an apolar amino acid;
 X_{15} is an acidic amino acid;
 X_{16} is a polar amino acid;
 X_{17} is a basic amino acid; and

each "—" between residues X₁ through X₁₇ is independently an amide, a substituted amide or an isostere of amide.

19. (Previously Added) The method of Claim 17, wherein:

X₁ is Gly;

X₂ is Trp or Ala;

X₃ is Asp or Ala;

X₄ is His;

X₅ is Met;

X₆ is Phe;

X₇ is Thr;

X₈ is Val;

X₉ is Asp or Ala;

X₁₀ is Phe;

X₁₁ is Trp;

X₁₂ is Thr;

X₁₃ is Ile;

X₁₄ is Met;

X₁₅ is Glu;

X₁₆ is Asn;

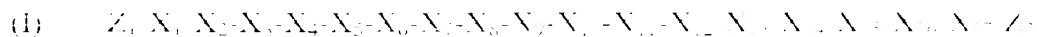
X₁₇ is His or Ala;

Z₁ is H₂N-;

Z₂ is -C(O)OH; and

each "—" between residues X₁ through X₁₇ is an amide linkage.

20. (New) A method of inhibiting TfR binding to transferrin, comprising administering to a subject a therapeutically effective amount of a compound comprising the formula:



wherein:

X₁ is an apolar residue;

X₂ is a hydrophobic residue;

X₃ is an acidic or an aliphatic residue;

X₄ is a basic residue;

X₅ is an apolar residue;

X_6 is an aromatic residue;
 X_7 is a polar residue;
 X_8 is an aliphatic residue;
 X_9 is an acidic or an aliphatic residue;
 X_{10} is an aromatic residue;
 X_{11} is an aromatic residue;
 X_{12} is a polar residue;
 X_{13} is Ile;
 X_{14} is an apolar residue;
 X_{15} is an acidic residue;
 X_{16} is a polar residue;
 X_{17} is a basic or an aliphatic residue;

Z_1 is H_2N- , $RHN-$ or, $RRN-$;

Z_2 is $-C(O)R$, $-C(O)OH$, $-C(O)OR$, $-C(O)NHR$, or $-C(O)NRR$;

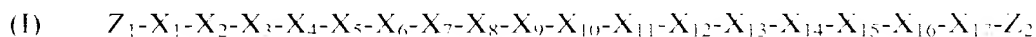
each R is independently (C_1-C_6) alkyl, (C_1-C_6) alkenyl, (C_1-C_6) alkynyl, substituted (C_1-C_6) alkyl, substituted (C_1-C_6) alkenyl or substituted (C_1-C_6) alkynyl;

each "—" between residues Z_1 and X_1 and residues Z_2 and X_1 represents a covalent linkage; and

each "—" between residues X_1 through X_{17} represents a covalent linkage,

wherein the compound reduces cell-associated binding of transferrin as measured in an *in vitro* cellular binding assay and produces at least an additive effect with soluble HFE/ β_2m heterodimers in reducing cell-associated binding of transferrin as measured in the assay.

21. (New) A method of treating an iron overload disease, comprising administering to a subject a therapeutically effective amount of a compound comprising the formula:



wherein,

X_1 is an apolar residue;
 X_2 is a hydrophobic residue;
 X_3 is an acidic or an aliphatic residue;
 X_4 is a basic residue;
 X_5 is an apolar residue;
 X_6 is an aromatic residue;

X₇ is a polar residue;
X₈ is an aliphatic residue;
X₉ is an acidic or an aliphatic residue;
X₁₀ is an aromatic residue;
X₁₁ is an aromatic residue;
X₁₂ is a polar residue;
X₁₃ is Ile;
X₁₄ is an apolar residue;
X₁₅ is an acidic residue;
X₁₆ is a polar residue;
X₁₇ is a basic or an aliphatic residue;
Z₁ is H₂N-, RHN- or, RRN-;

Z₂ is -C(O)R, -C(O)OH, -C(O)OR, -C(O)NHR, or -C(O)NRR;

each R is independently (C₁-C₆) alkyl, (C₁-C₆) alkenyl, (C₁-C₆) alkynyl, substituted (C₁-C₆) alkyl, substituted (C₁-C₆) alkenyl or substituted (C₁-C₆) alkynyl;

each "—" between residues Z₁ and X₁ and residues Z₂ and X₁₇ represents a covalent linkage; and

each "—" between residues X₁ through X₁₇ represents a covalent linkage,

wherein the compound reduces cell-associated binding of transferrin as measured in an in vitro cellular binding assay and produces at least an additive effect with soluble HFE/ β_2 m heterodimers in reducing cell-associated binding of transferrin as measured in the assay.